



(Billing Code: 4150-31)

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Office of the Secretary

Findings of Research Misconduct

AGENCY: Office of the Secretary, HHS

ACTION: Notice.

SUMMARY: Notice is hereby given that the Office of Research Integrity (ORI) has taken final action in the following case:

Bryan William Doreian, Ph.D., Case Western Reserve University: Based on the admission of the Respondent, ORI found that Dr. Bryan William Doreian, former postdoctoral fellow, Department of Dermatology, Case Western Reserve University (CWRU), engaged in research misconduct in research supported by National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH), grant T32 HL07887 and National Institute of Neurological Disorders and Stroke (NINDS), NIH, grant R01 NS052123.

ORI found that the Respondent engaged in research misconduct by falsifying data that were included in:

- Doreian, B.W. “Molecular Regulation of the Exocytic Mode in Adrenal Chromaffin Cells.” Submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, August 2009; hereafter referred to as the “Dissertation.”
- Doreian, B.W., Fulop, T.G., Meklenburg, R.L., Smith, C.B. “Cortical F-actin, the exocytic mode, and neuropeptide release in mouse chromaffin cells is regulated by myristoylated alanine-rich C-kinase substrate and myosin II.” *Mol Biol Cell*. 20(13):3142-54, 2009 Jul; hereafter referred to as the “*Mol Biol Cell* paper.”
- Doreian, B.W., Rosenjack, J., Galle, P.S., Hansen, M.B., Cathcart, M.K., Silverstein, R.L., McCormick, T.S., Cooper, K.D., Lu, K.Q. “Hyper-inflammation and tissue destruction mediated by PPAR- γ activation of macrophages in IL-6 deficiency.” Manuscript prepared for submission to *Nature Medicine*; hereafter referred to as the “*Nature Medicine* manuscript.”

As a result of the Respondent’s admission, the Respondent will request that the following paper be retracted: *Mol Biol Cell*. 20(13):3142-54, 2009 Jul.

ORI finds that Respondent falsified numerical values in the *Mol Biol Cell* paper, the submitted *Nature Medicine* manuscript, and the Dissertation by altering the number of samples or the experimental results to improve the statistical results. Specifically, ORI finds that Respondent:

1. falsified the quantification of immunofluorescence for the ratio of phosphorylated to unphosphorylated MARCKS protein in response to different stimuli in Figure 2 of the *Mol Biol Cell* paper and in Figure 12 of the Dissertation by falsifying the sample number as $n=15$
2. falsified the quantification of immunofluorescence for filamentous actin in response to different stimuli in Figure 3 of the *Mol Biol Cell* paper and in Figure 13 of the Dissertation by falsifying the sample number as $n=15$
3. falsified the quantification for the effect of blebbistatin on catecholamine release as determined by patch clamp analysis in Figure 22 of the Dissertation by stating that 14 cells had been assayed when only 8 cells had been assayed
4. falsified the Pearson's cross-correlation analysis in Figure 7 of the *Mol Biol Cell* paper and in Figure 25 of the Dissertation, used to calculate the degree of spatial correlation between pan-chromogranin A/B (CgA/B) and the endosomal membrane, by stating that 20 or more cells had been tested for each condition when only 9-18 cells had been tested for each condition
5. falsified RT-PCR values for iNOS and TNF-alpha expression recorded on spreadsheets and presented in Figures 5e and 5f of the *Nature Medicine* manuscript showing the effect

of hyper-inflammatory macrophage generation on tissue destruction, by falsifying the numeric values to fit the hypothesis of the manuscript

6. falsified ELISA graphs for the concentration of TNF- α in the aAB IL-6 mice and their controls in Figure 6j of the *Nature Medicine* manuscript showing the effect of rosiglitazone treatment in the mice, by multiplying the experimental values by 100 to match the magnitude of the values presented in Figures 2i, 6h, and 6i of the *Nature Medicine* manuscript
7. falsified the RT-PCR results presented in the *Nature Medicine* manuscript for quantification of iNOS and TNF- α RNA expression by claiming that the results represent the rmean of three identical experiments when the three experiments were normalized differently to yield the desired result. Specifically, false results were presented for peritoneal macrophages treated in vivo with rosiglitazone and/or inhibitors of PPAR γ signaling Figures 1g, 1h, and 1i, and for iNOS RNA expression in IL6^{-/-} macrophages treated in vitro with either SOCS3 antisense oligonucleotides in Figure 2g or the STAT3 decoy in Figure 2j.

Dr. Doreian has entered into a Voluntary Settlement Agreement and has voluntarily agreed for a period of three (3) years, beginning on January 15, 2013:

- (1) to have his research supervised; Respondent agreed that prior to the submission of an application for U.S. Public Health Service (PHS) support for a research project on which his participation is proposed and prior to his participation in any capacity on PHS-supported research, Respondent shall ensure that a plan for supervision of his duties is submitted to ORI for approval; the supervision plan must be designed to ensure the scientific integrity of his research contribution; he agreed that he shall not participate in any PHS-supported research until such a supervision plan is submitted to and approved by ORI; Respondent agreed to maintain responsibility for compliance with the agreed upon supervision plan;
- (2) that any institution employing him shall submit, in conjunction with each application for PHS funds, or report, manuscript, or abstract involving PHS-supported research in which Respondent is involved, a certification to ORI that the data provided by Respondent are based on actual experiments or are otherwise legitimately derived and that the data, procedures, and methodology are accurately reported in the application, report, manuscript, or abstract;
- (3) to exclude himself voluntarily from serving in any advisory capacity to PHS including, but not limited to, service on any PHS advisory committee, board, and/or peer review committee, or as a consultant; and

- (4) to request that the following paper be retracted: *Mol Biol Cell*. 20(13):3142-54,
2009 Jul.

FOR FURTHER INFORMATION CONTACT:

Director
Office of Research Integrity
1101 Wootton Parkway, Suite 750
Rockville, MD 20852
(240) 453-8200

David E. Wright,
Director
Office of Research Integrity

[FR Doc. 2013-02487 Filed 02/04/2013 at 8:45 am; Publication Date: 02/05/2013]